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Abstract

Schematic knowledge about individual people enables us to predict and understand their behaviour in novel situations. The ventromedial prefrontal cortex (vmPFC) and hippocampus have been identified as playing key roles in schema-based processing of new experiences. Nevertheless, their precise roles and their interactions with each other remain poorly understood. We manipulated schematic knowledge by familiarising participants to the lead characters of one of two TV shows, both of which featured young couples. Familiarisation involved watching episodes of the show over a period of at least a week. Then participants viewed pictures of all 4 characters in an MRI scanner and performed a recognition memory test afterwards. They also performed a memory test for short novel videos from the two shows. Schematic knowledge boosted performance on both of the memory tests. Whole-brain analyses revealed that schematic knowledge increased activation in the vmPFC and the retrosplenial cortex, while a region-of-interest analysis additionally found increased activity in the hippocampus. The size of the effects in the vmPFC and hippocampus were not significantly different. Representational similarity analyses found evidence for person-specific patterns of activity in the vmPFC but not hippocampus, but neither region showed an effect of training on representational similarity. Our findings suggest complementary roles for the vmPFC and hippocampus in processing schematic knowledge that has been recently acquired over multiple occasions.

Introduction

The world and people around us can be confusing. To understand what is happening in our environment we rely on our prior schematic knowledge. Schemas are abstracted knowledge structures learned over multiple episodes (Ghosh & Gilboa, 2014; see for review Gilboa & Marlatte, 2017). A schema for a well-known friend might include their appearance, likes and dislikes and their personality traits. This knowledge helps us understand and predict other peoples' behaviour in new situations (Ramon & Gobbini, 2018). The present study investigates the impact of schematic knowledge - acquired in a naturalistic manner - on both episodic memory processes and on brain activity in regions that support these processes. In this introduction, we will first highlight the findings from different types of studies that have been used to investigate the brain-basis of schematic knowledge. We will then summarise current views on how schematic processing is carried out in the brain before introducing the current study.

A range of tasks have been used to examine the neurobiology of schemas. These fall broadly into three different types. The first are studies that rely on participants' pre-existing knowledge, contrasting behavioural and physiological responses to stimuli that are familiar versus unfamiliar (Bein et al., 2014; di Oleggio Castello et al., 2017; Liu et al., 2016; McAndrews et al., 2016; van Kesteren et al., 2013; van Kesteren et al., 2014). For example, Liu et al., (2016) required participants to learn face-house associations, where the faces were of either famous or non-famous people. Such studies consistently find positive effects of prior knowledge on memory performance. It has been argued that this boost in performance is due to the rich associations that exist for familiar items which enables new memories to be organised efficiently as well as increasing the distinctiveness of individual items (e.g. Bird et al., 2011; Van Overschelde et al., 2005).

The second class of studies involve teaching participants new arbitrary rule-based associations (Schlichting et al., 2015; Schlichting & Preston, 2016; Sommer, 2016; Wagner et al., 2015; Zeithamova et al., 2012). In one such study, Sommer and colleagues (2016) trained participants on 10 distinctive object-location arrays each containing 20 locations. During training, only some of the locations in each array were associated with an object. Participants were then presented with novel object-location pairs that were either related or unrelated to the previously learned spatial structure. In these types of paradigms, memory is better for new items that conform to the learnt rules.

The last types of studies use naturalistic video- or text-based tasks and expose participants to information that aids the interpretation of novel events (e.g. Ames et al., 2015; Keidel et al., 2017; Kesteren et al., 2010; Raykov et al., 2018). In a study by van Kesteren et al., (2010), participants watched a movie for which prior knowledge was manipulated. On the first day of the experiment participants watched the first part of the movie in either scrambled or unscrambled order. On the next day both groups watched the last 15 minutes of the movie in unscrambled order. Thus, participants who had watched the unscrambled first half of the movie had a more coherent knowledge base within which to interpret the second half clip. Once again, the provision of knowledge consistently results in improved memory for the subsequent movie or narrative text.

All the studies mentioned above have combined manipulations of prior knowledge with functional MRI to investigate the brain regions involved schema processing. Overall there is a general consensus that when participants engage schematic knowledge, brain activity is modulated in certain key regions. These are the ventromedial prefrontal cortex (vmPFC) and hippocampus, as well as other regions such as the anterior temporal lobes, posterior midline regions, and - particularly in the case of faces - the fusiform gyrus (see Gilboa & Marlatte, 2017). Despite this overarching similarity across studies, there is still inconsistency in the specific pattern of BOLD activity effects. For example, whereas some studies find that processing stimuli related to prior knowledge is associated with higher activity in vmPFC and hippocampus (e.g. di Oleggio Castello et al., 2017; Liu et al., 2016; Sommer, 2016; Zeithamova et al., 2012), other studies find a different pattern showing that the hippocampus is more active whilst processing schema-incongruent associations (McAndrews et al., 2016; van Kesteren et al., 2013, see also van Kesteren et al., 2014). For instance, using paradigms reliant on pre-experimental knowledge, Liu et al., (2016) found that known faces engaged both the vmPFC and hippocampus, but van Kesteren et al., (2013) found that while schema-consistent associations activated medial PFC, the hippocampus was more active when viewing schema-inconsistent associations. While the former result suggests that the two regions are part of a single functional unit, the later finding suggests that the two regions play distinct roles (for reviews see Ghosh & Gilboa, 2014; Gilboa & Marlatte, 2017; McCormick et al., 2018; Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017; van Kesteren et al., 2012).

Various theoretical frameworks have been proposed to explain how different brain regions interact during schema-based processing of new information. Van Kesteren and colleagues proposed the “SLIMM” framework ("Schema-Linked Interactions between Medial prefrontal and Medial temporal lobes”, van Kesteren et al., 2012). SLIMM proposes that the vmPFC and hippocampus have competing roles in the presence of prior knowledge (see also Greve et al., 2019). According to this framework, incoming information congruent with prior knowledge is associated with increased medial PFC engagement and inhibition of medial temporal lobe (including hippocampal) activity. By contrast, processing information incongruent with prior knowledge should be associated with increased hippocampal activity. However, other models suggest that the hippocampus and medial PFC play complementary roles in relating new experiences with prior knowledge (e.g. Preston & Eichenbaum, 2013). In a recent formulation, Robin and Moscovitch (2017) argued that the posterior hippocampus, anterior hippocampus and vmPFC play roles in processing detail, gist and schema information respectively, and that these regions act cooperatively when retrieving episodic memories.

The lack of consensus in the roles different brain regions play in schema processing is unsurprising, given the variability in findings from different fMRI studies. It is possible that some of this variability is a consequence of the paradigms used. Studies that capitalise on schematic knowledge acquired outside of the laboratory have a strength in that the knowledge is acquired in real-world settings. However, it is difficult to equate the amounts of information known about the different stimuli across participants. Consequently, the type, and richness, of information activated by a “familiar” stimulus is likely to be highly variable (see also Westmacott

& Moscovitch, 2003). Studies that require the learning of rule-based schemas enable careful control of the amount of schema-relevant information learnt, but the schemas involve highly abstract information and the rules are often learnt rapidly in one or two sessions close to when scanning takes place. This is very different from real-world situations where schematic knowledge is acquired over weeks, months and years. Lastly, paradigms that manipulate knowledge of a single event or narrative are not necessarily targeting the more general and abstract schematic knowledge that is acquired over multiple episodes.

For these reasons, the present study uses a novel method to acquire new schematic knowledge under a naturalistic, yet carefully controlled, training regime. Over the course of a week, participants watched six episodes from one of two television shows. This allowed participants to gradually build up their knowledge of the show's main characters across multiple episodes over several days, in a manner similar to our acquisition of person-specific semantic knowledge in everyday situations. Both shows were US situation comedies (henceforth, "sitcoms") that aired in the early 1990's and were previously unfamiliar to our participants. The trained show was counter-balanced across participants to control for potential stimulus-specific confounds between the two shows. Before scanning, we checked that all participants had complied with the training regime by examining their memory for the training videos.

The main purpose of the study was to identify the brain regions that are engaged when schematic knowledge is activated. Familiar faces are thought to automatically activate "identity-specific semantic codes" (Bruce & Young, 1986). We therefore assume that after training, participants will spontaneously activate their schematic knowledge about the characters when viewing them in both static photos and short video clips. We therefore contrast the BOLD response when people view pictures of the trained characters compared to when they view characters from the untrained show. To engage participants in the in-scanner task and to obtain an index of schematic knowledge, participants performed a recognition memory test for the specific pictures they viewed in the scanner. Participants also watched and then answered questions about short video clips taken from unseen episodes of both sitcoms. Although these tasks do not directly assess schematic knowledge learnt about the trained characters, numerous studies have demonstrated a memory advantage for memoranda associated with pre-existing schematic knowledge (e.g. Bird et al., 2011; Klatzky & Forrest, 1984; Liu et al., 2016).

We carried out three types of analyses. Univariate analyses investigated differences in overall brain activity for pictures of familiarised versus unfamiliar characters. Differences could reflect the direct effects of activation of schematic information or related processes (such as activation of episodic memories involving the characters or the rewarding effects of seeing a familiar person). Multivariate representational similarity analyses (RSAs) aimed to identify regions where person-specific information was represented – and critically, regions where person-specific representations existed only for the trained characters. Lastly, functional connectivity analyses were used to identify whether the connectivity between different brain regions was modulated by the presence of schematic knowledge about the characters. Our analyses focussed particularly on effects within and between the vmPFC and hippocampus. We predicted schema-related effects due to

training in the vmPFC. Additional training-related effects within the hippocampus would be supportive of views that the vmPFC and hippocampus work in concert when prior knowledge can support new learning (Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017). By contrast, stronger engagement of the vmPFC compared to the hippocampus for trained material would be more in line with the SLIMM model.

Methods

Participants

Thirty right-handed native English speakers (15 female), between ages 18-29 (21.71 ± 3.08) were included in the experiment. One participant was not included in the fMRI analysis, as they did not complete the task due to a technical issue with the scanner. One additional person was excluded from the behavioural analysis of the video memory test due to a technical issue. Before taking part, participants were screened to be unfamiliar with other shows/films where the main characters played a major role. Informed consent was obtained from all participants and they were all paid £40.

Stimuli

Sixty-four colour pictures taken from two US shows ("Mad about you" - MaD and "Dharma and Greg" - DG) were used in the scanning session. The shows were chosen to be previously unfamiliar to our participants. Both shows represent fictional situations happening in the everyday life of a couple in their 30s living in USA. There were 16 pictures for each of the four main characters (two for each show). The pictures were selected from unseen clips from the shows. Each picture represented a single character in the living room or in the kitchen. The camera angle and clothes differed across pictures of the same character. 10 short videos for each show were also used for a memory test. Videos from MaD show (32.7secs ± 6.73) were on average the same duration as videos from the DG show (33.4secs ± 7.87) ($p = .833$). The videos were selected from previously unseen episodes and represented self-contained situations happening in unfamiliar locations (e.g. the museum). All clips were presented in black and white and the audio was scaled to the same mean decibel intensity with Praat (version 6.0.15).

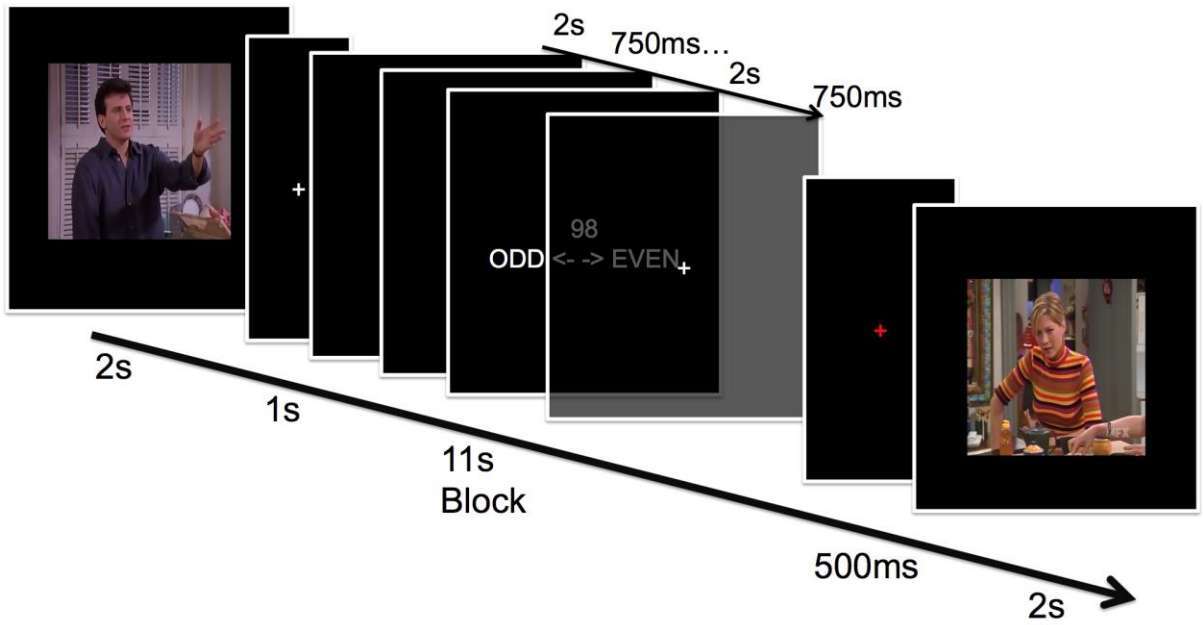

Figure 1 *Schematic of picture task*. Participants viewed pictures of the 4 main characters taken from unseen episodes from two TV shows. Before the experiment participants were familiarised with one of the shows (2 of the characters). Each picture represented only one character in their kitchen or living room. The view angles and clothes of the characters differed across different pictures. Participants made an odd-even number judgment task in between presentation of pictures, which acted as an active baseline task.

Procedure

Participants were asked whether they had seen either of the two shows or other shows including the same actors in leading roles. Participants who reported seeing either of the shows (or shows with the same actors in main roles) were not included in the experiment. Participants were then randomly assigned to one of the two training conditions (MaD or DG). This counterbalancing allowed us to control for stimuli effects at the group level. Each participant was allocated 6 episodes to watch at their own time. Participants were asked to watch the episodes over a week rather than binge watch all episodes in one sitting. To ensure participants followed the instructions their memory for the 6 training episodes was tested before continuing with the scanning session. Participants freely recalled the 6 episodes. When necessary, cues were provided for certain details (e.g. what was said, the intentions and emotions of the characters, their location) about scenes in the episodes. Participants that required many cues and could not recall specific details about one or more episodes were asked to re-watch them. Only one of the included participants needed to re-watch a single episode. This screening procedure was done at least 2 days before scanning and took approximately 45 minutes.

Participants carried out 4 functional runs within the scanner; 2 runs involved viewing pictures (run 1 and run 4) and 2 runs involved watching short videos (runs 2 and 3). Each run of the picture task lasted 9 minutes and participants saw 8 pictures for each of the 4 main characters (2 characters from the trained and 2 from the untrained show). Presentation order was randomized within runs. Each picture was

presented for 2 seconds on a black background followed by a 12 second inter-stimulus-interval during which participants made an odd/even judgment, which served as active baseline task (Stark & Squire, 2001; Visser et al., 2010). See Figure 1 for a schematic of the procedure. The odd/even task comprised a sequence of four numbers randomly chosen from the range 1-98. Each number was presented for 2 seconds followed by a fixation cross lasting 750 milliseconds. A red fixation cross was presented for 500 milliseconds before the presentation of the next picture. Participants were informed their memory for the pictures would be tested outside of the scanner. To further ensure participants attended to the pictures, there was an oddball target detection task where participants pressed a target if they saw a picture of an adult older than the 4 repeated characters (4 targets per run). Each run of the video task lasted approximately 16 minutes. Ten videos were presented in each of the two video task runs (5 trained, 5 untrained). Videos were presented in an interleaved order. There was a 13 second inter-trial interval between each video.

Outside of the scanner participants first completed a memory test for video task. We used a three-alternative forced-choice test for the details from the video (see Supplementary Fig. 2). There were 5 questions for each video. The sets of 5 questions were presented in a pseudo-random order so that there were no more than 3 sets of questions in a row for the same show. Performance was measured as the proportion correct, with chance level being 0.33. We report the behavioural data from the video memory test below. The fMRI data collected during these runs is the focus of a separate manuscript and will not be described further here.

Participants then completed a yes/no recognition memory test with 40 old (studied) pictures and 62 new (unstudied) pictures. The new pictures were selected from previously unseen episodes. Each picture was presented for 5 seconds or until the participants made a response. A white fixation cross was presented for 2 seconds between each picture and a red fixation cross preceded the next picture by 400 milliseconds. To characterise performance, whilst accounting for response bias, we used the non-parametric discrimination index A' (Snodgrass et al., 1985). The index was calculated separately for each participant for the trained and untrained pictures. The index was calculated as 0.5 + ((H - FA)*(1 + H - FA))/4*H*(1-FA), where H stands for hits - correct old responses to previously presented pictures, and FA stands for false alarms - incorrect old responses to new pictures. A' ranges from 0-1 and 0.5 indicates chance level performance.

Behavioural analysis

For both the video and pictures task accuracy on the trained and untrained stimuli was compared using a paired samples t-test.

MRI acquisition

A 3T Siemens Prisma scanner with a 32-channel head-coil was used to acquire all images. Soft cushions were inserted into the head coil to minimize head movement. Functional images were acquired with a gradient-echo EPI sequence with multiband acceleration factor of 8 with the following parameters (TR = 0.8 seconds; TE = 33.1 ms; 52 degree flip angle; FOV = 208x180mm; 72 slices with sliced thickness of 2mm and isotropic 2mm voxels). Two SpinEcho Field map runs

with reversed phase-encode blips in both Anterior to Posterior and Posterior to Anterior were acquired with the same parameters as the functional images. A high-resolution structural T1-weigthed image was acquired with 3D MPRAGE sequence (TR = 2.4 seconds; TE = 2.14 seconds; 8 degree flip angle; FOV = 224x224mm and 0.8mm isotropic voxels).

Image pre-processing

All images apart from the field maps were pre-processed with SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK). Images from both runs were initially spatially realigned to the mean image. Field maps were estimated and applied to the motion corrected data with command-line functions from FSL (Smith et al., 2004). Field maps were used to correct for image distortions (Andersson et al., 2001; 2003). The anatomical image was coregistered to the mean functional image and segmented into grey, white and cerebrospinal fluid using tissue probability maps. The segmented images were used to estimate deformation fields, which were applied to the functional data to transform them to MNI space. A 6mm FWHM smoothing kernel was applied to the functional images for the whole-brain GLM analyses.

Data analysis

Data were analysed with SPM 12, the CosMoMVPA toolbox (Oosterhof et al., 2016) and custom scripts in MATLAB (Version 2017b, The MathWorks, Inc., Natick, MA, USA). All analyses were conducted on MNI normalised images. The RobustWLS toolbox in SPM 12 was used to estimate the first level models (Diedrichsen & Shadmehr, 2005). This method downweights volumes with high variance estimates, which leads to a "soft" exclusion of bad volumes. We used the Bspmview toolbox (www.bobspunt.com/bspmview) to visualise and describe our data. The toolbox implements MNI coordinates from the Anatomical Automatic Labelling 2 toolbox for SPM 12.

Whole-brain analyses

We first carried out whole-brain random-effect analyses across participants. Contrast images in MNI space were evaluated with one-sample t-tests. Results were thresholded in SPM using a cluster-level family-wise error correction ($p < .05$), with a cluster-defining voxel threshold of $p < .001$.

ROI definition and analyses

Predefined ROIs were used in follow-up analysis, as a seed for functional connectivity analysis and for representational similarity analysis. These ROIs were in the hippocampus and the vmPFC.

We investigated separately the head, and the combined body and tail, of the hippocampus since theories of schematic processing have suggested differentiation between these sub-regions of the hippocampus (Preston & Eichenbaum, 2013; Ritchey et al., 2015; Robin & Moscovitch, 2017). These regions were defined based on a segmentation carried out by Ritchey and colleagues (2015) and available at

www.neurovault.org. This ROI was used for (1) univariate activity analyses, (2) functional connectivity, and (3) representational similarity analysis.

In order to compare activations between vmPFC and hippocampus, while avoiding circular voxel selection, we used a leave-one-participant out (LOSO) method (Esterman et al., 2010). The voxels for an vmPFC ROI for a given participant were identified by using the suprathreshold voxels in a whole-brain group analysis that excludes the participant. For instance, the ventromedial prefrontal cortex ROI for participant 1 is identified from suprathreshold voxels from a group analysis of all the other participants excluding participant 1. This was repeated for each participant.

We also used an anatomical mask of the ventromedial prefrontal cortex to perform representational similarity analysis (RSA). We used the WFU atlas pick toolbox and the AAL to identify ventromedial prefrontal cortex following the procedure presented in Liu (2016). The ventromedial mask included the left and right gyrus rectus and the left and right medio-orbital section of the frontal cortex.

GLM analysis

For the univariate analyses we modelled all of the trained pictures (32 trials) with a single regressor and a separate regressor included the information about the untrained characters (32 trials). We also included a regressor of no interest for the odd-ball pictures and modelled the six motion parameters. To estimate patterns to use in the subsequent RSA we modelled each of the characters with a single task regressor (Trained male, Trained female, Untrained male, Untrained female; 8 trials per run per character). This meant that a regressor for a character included pictures of the same character in different locations and from different viewpoints. We implemented a slow event related design, which allowed us to sample the whole duration of the HRF and we used multiple trials per character to estimate robust patterns for each character (Zeithamova et al., 2017). Estimated patterns for all four characters were used in the general identity and trained vs untrained RSAs. An additional regressor of no interest was used for the oddball images. The odd/even judgment task was not modelled and served as an implicit baseline. The six motion parameters, mean session effects, and a high pass filter with a cut-off of 1/128 Hz were also included in the models. The contrasts of interest from the first-level models were subjected to a group analysis.

To compare BOLD activity between the hippocampal and vmPFC ROIs whilst accounting for regional differences and across-participants variability of the BOLD signal we computed a differentiation index (see Koen et al., 2019). For each trial and for each separate ROI we extracted the mean signal over all voxels within the ROI. Thus, we had a single value for each ROI and each condition. This allowed us to compute a differentiation index separately for each ROI. The individual trial values were used to estimate the mean (μ) and variability (σ^2) for each condition (trained and untrained). Positive values of the differentiation index indicate the ROIs preference for the trained versus the untrained condition. The differentiation index was calculated with the following formula:

$$\text{Differentiation Index} = \frac{\mu_{trained} - \mu_{untrained}}{\sqrt{\frac{\sigma^2_{trained} + \sigma^2_{untrained}}{2}}}$$

Connectivity analyses

Based on prior findings of modulated connectivity in the hippocampus when processing schematic knowledge (van Kesteren et al., 2010) we ran generalized psychophysiological interaction (gPPI) analysis (McLaren et al., 2012) to examine whether the anterior (head) and/or posterior (combined body and tail) hippocampus would show connectivity with the rest of the brain that is modulated by prior knowledge. We also used the significant vmPFC cluster as a seed to examine whether there are changes in connectivity modulated by training over and above the increased univariate response in the vmPFC.

Representational similarity analysis (RSA)

We ran exploratory RSAs (Kriegeskorte et al., 2008) to investigate whether activation patterns were specific to the identities of the four main characters presented and whether pattern similarity was modulated by training. Whole-brain searchlight analyses were performed using a searchlight sphere with radius of 4 voxels (mean 235 voxels). Images for the RSAs were pre-processed as described above but were not smoothed before estimating the first-level models. All RSAs were performed for each subject separately in normalized space and the resulting maps were subjected to a one-sample group t-test against zero.

For each searchlight sphere, the multi-voxel response patterns (*t*-statistics) for each character for run 1 and run 2 were extracted and vectorised to compute their similarity using Pearson correlation. The resulting correlation coefficients were then Fisher transformed and assigned to the center voxel of each searchlight sphere. The resulting matrix of 16 correlations represents the neural similarity between the four characters across the two runs. The four diagonal values representing the matching identities across runs and the 12 off-diagonal values representing the correlations between non-matching identities (see Fig. 2).

To identify brain regions that show higher similarity for matching identities we compared the correlation matrices calculated above with the similarity matrix shown in Fig. 2 (left). This is equivalent to computing the mean average similarity for matching identities minus the mean average similarity for non-match identities ('Identity RSA').

A second RSA compared only the similarities of the matching identities to investigate brain regions where similarity was greater for the trained characters compared to the untrained characters (see Fig. 2, right; 'Trained versus untrained RSA').

It is possible that any observed similarity to characters could be driven in part by the background scene (e.g. the character Dharma was always pictured in her

living room or kitchen, but never the rooms from the other show). To ensure any observed effects are specific to character identity an additional RSA was run to examine the similarity across matching locations versus mismatching locations, irrespective of the character in the picture. There were two locations within each show (kitchen and living room). The first-level models included a single regressor for each of the all four locations (trained kitchen, trained living room; untrained kitchen; untrained living room) in each run. The regressor trained kitchen averaged over pictures of the trained characters in the kitchen. The similarity matrix was the same as the Identify RSA, but the patterns were specific to the locations rather than the characters. We also ran an RSA comparing the similarity for the trained and untrained locations.

In addition to whole-brain searchlight analyses we ran the RSAs described above in the hippocampal and vmPFC ROIs using all voxels within the ROI as activity patterns.

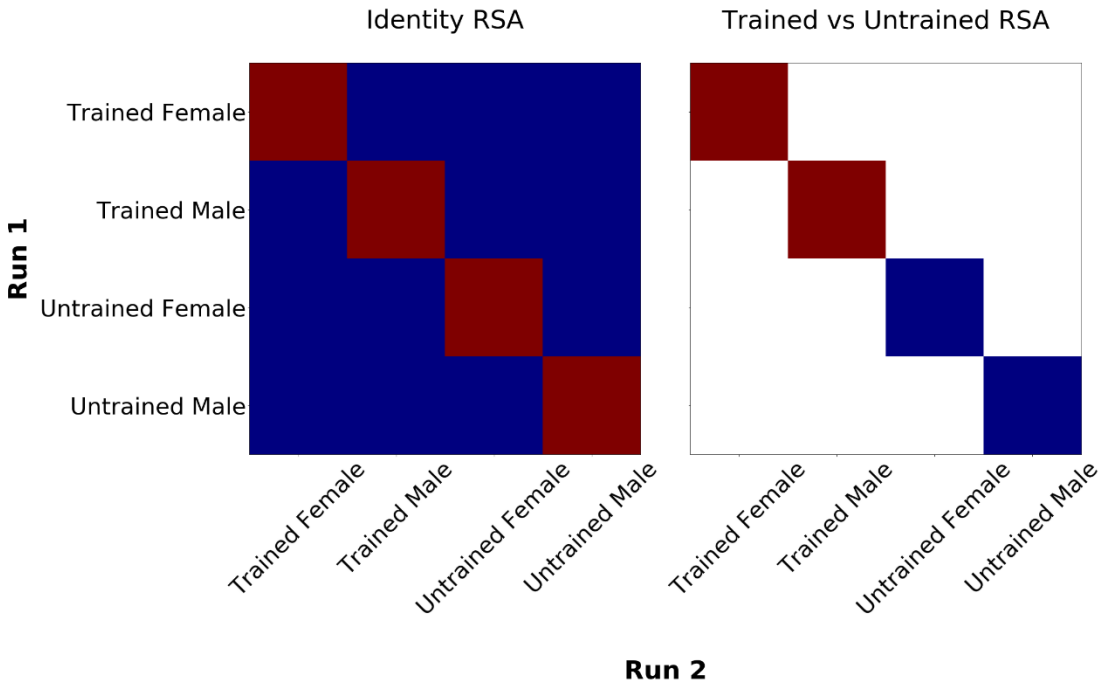

Figure 2 *Contrast Matrices.* The contrast matrixes used for the RSA analyses are shown above. Red indicates positive and blue indicates negative contrast values. In the identity RSA the main contrast was comparing for higher similarity for matching identities (across runs) versus mismatching identities. The second analysis examined modulations by training and which regions show more similar patterns (across runs) for the trained matching identities versus the untrained matching identities

Results

Behavioural Results

In the pictures task participants showed higher old/new discrimination, measured with A' (Snowgrass et al., 1985), for the trained pictures compared to the untrained ones (t_{28} = 2.07; p = 0.047) (see Fig. 3). This effect is in line with previous findings of better recognition of familiar faces (Bird et al., 2011; Klatzky & Forrest, 1984). Overall, accuracy on the video memory questions was high (mean = 0.75 SD = 0.11 chance level = 0.33). Consistent with the results from the recognition memory test, performance on the video memory test was higher for the clips taken from the trained show (mean = 0.78) versus the untrained show (0.72: t_{27} =3.5; p = 0.002).

Participants showed high overall performance on the odd-even task in the scanner with average accuracy of 97% (sd = 0.02). There were no differences in accuracy or reaction times on the odd-even task trials following the trained or untrained pictures (ps > 0.42).

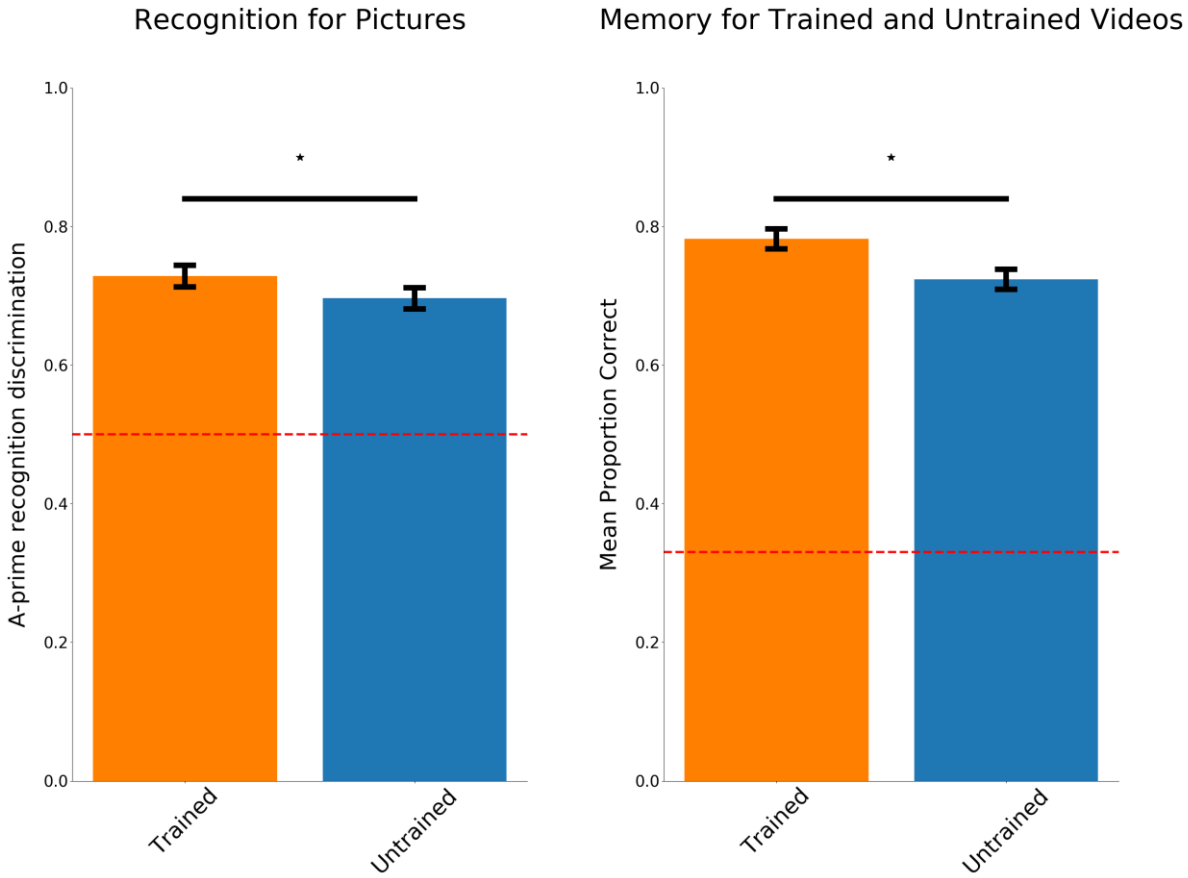

Figure 3 *Behavioural results*. Bar graph shows discrimination performance on the picture task, memory accuracy for the videos. Both measures were significantly higher for the trained show. Bar graph shows mean and standard error. Red dashed line indicates chance performance for each of the two tests. The star indicates a significant difference between the trained and untrained conditions at p < 0.05.

Imaging results

Univariate analyses

The contrast of viewing pictures versus the odd-even baseline task showed extensive activations including visual cortex, anterior temporal poles, ventromedial prefrontal cortex (vmPFC) and hippocampus (see Supplementary Figure 1).

In our main univariate analysis of interest, we compared activity while participants viewed the trained versus the untrained characters. The revealed whole-brain significant increases in BOLD activity in the vmPFC (cluster size = 185; peak voxel x = -4, y = 42, z = -12 t_{28} = 5.35) and RSC (cluster size = 183; peak voxel x = 12, y = -48, z = 18; t_{28} = 5.06)(see Fig. 4).

Apart from whole brain effects we also focused on a priori defined regions of the anterior and posterior hippocampus. We examined the average BOLD response within our ROIs over all voxels. The head (t_{28} = 2.42, p = 0.02) and the body (including tail; t_{28} = 2.49; p = 0.02) of the hippocampus showed higher activations for the trained versus the untrained characters.

We were particularly interested to examine if there were any differential effects in processing pictures of trained versus untrained people between the vmPFC and the hippocampus. The vmPFC region maximally sensitive to the trained versus untrained effects was identified using a LOSO method (see above). Effects in this region were compared to the effects in the head and body of the hippocampus using the differentiation index method (for details see Methods). The across regions repeated ANOVA did not show any significant difference in differentiation index method across regions ($F_{1,83}$ = 0.95, p = 0.33)(see Fig. 5).

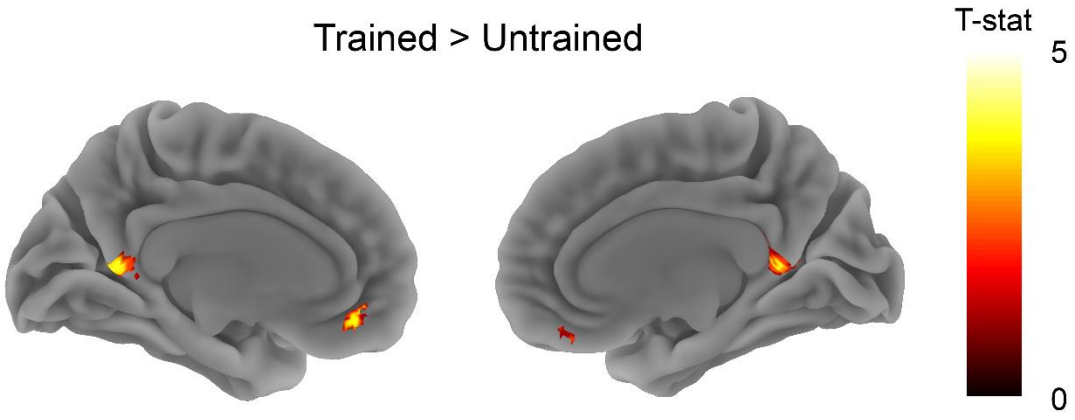

Figure 4 *Trained vs Untrained pictures***.** The maps shows brain regions more active for the trained pictures when compared to the untrained pictures. Map is thresholded at p < 0.001 with FWE cluster size correction.

Connectivity analyses

Contrary to our expectations, we did not observe any modulation of hippocampal connectivity by our training manipulation. Additionally, we did not observe any differences in connectivity between training conditions when we used the significant vmPFC cluster as a seed. Our result is in line with a recent finding from Brod and colleagues (2016) who also did not observe significant modulation of connectivity of hippocampus and vmPFC (but see Liu et al., 2016).

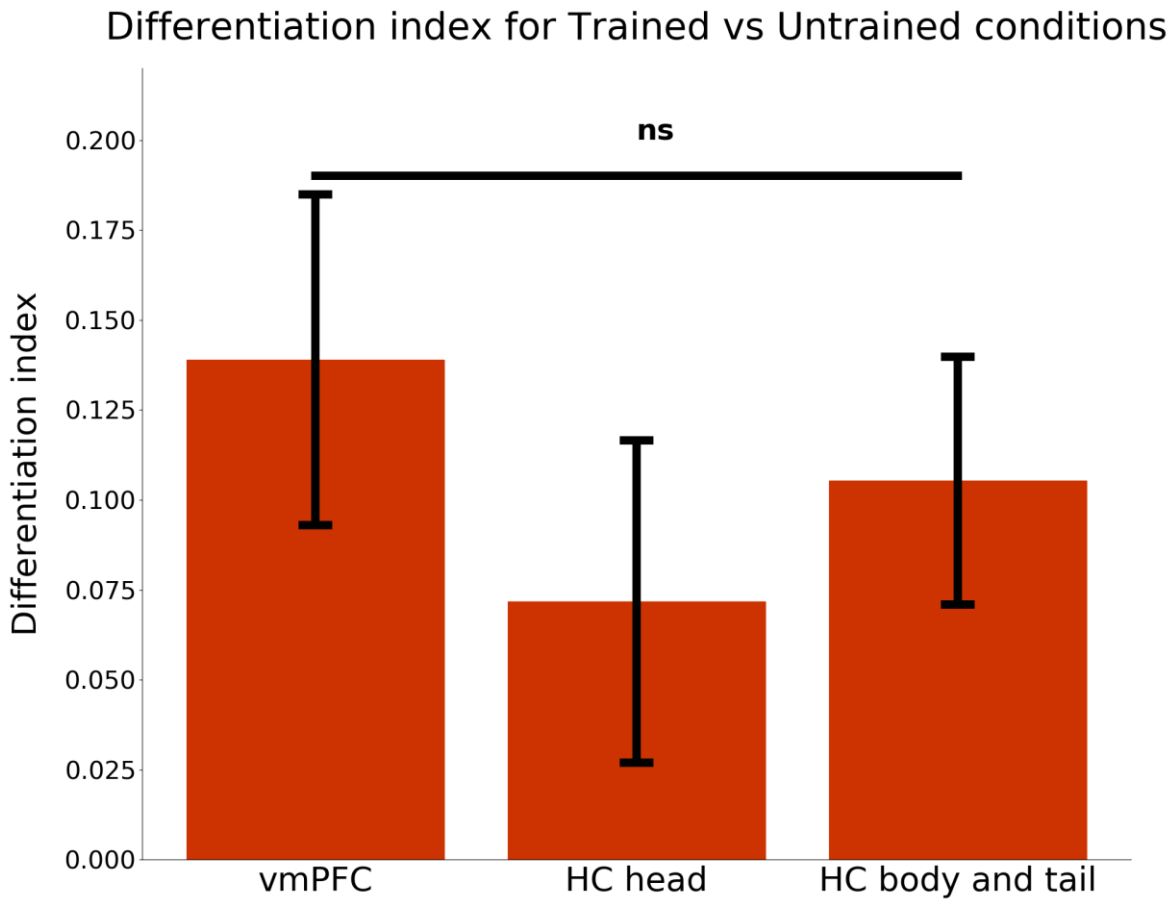

Figure 5 *Within ROI Trained vs Untrained differentiation index*. The plot shows the average differentiation index in the vmPFC, head of the hippocampus (HC head) and body plus tail of the hippocampus (HC body and tail). A positive differentiation index indicates that the regions shows greater activation for the trained condition. Bar graph shows mean and standard error.

RSA

The Identity RSA searched for brain regions that showed consistent local patterns of activity for the four different characters. This analysis revealed a significant cluster in the vmPFC (cluster size = 273; peak voxel x = -10, y = 38, z = -2; t_{28} = 5.46), a cluster in the occipital cortex (cluster size = 264; peak voxel x = 16, y = -90, z = 16; t_{28} = 5.34), and a smaller cluster in the right occipital cortex (cluster size = 98; peak voxel x = 36, y = -72, z = -4; t_{28} = 4.69) (see Fig. 6). A follow-up RSA

for locations did not reveal any significant effects across the brain, suggesting that the Identity-RSA results are driven by the characters themselves and not the locations that they are pictured in.

The Trained vs Untrained RSA revealed a single cluster in the left inferior temporal gyrus (cluster size = 79; peak voxel x = -40, y = -44, z = -12; t_{28} = 4.98) where activity patterns were more similar for the characters for whom schematic knowledge was available (see Fig. 7). The location of this cluster corresponds to the well characterised fusiform face area. When comparing similarity for trained and untrained locations at the whole brain level we found a significant cluster in left postcentral gyrus (cluster size = 134; peak voxel x = -20, y = -42, z = 66; t_{28} = 5.74).

In addition to whole brain searchlight analysis we ran both the Identity RSA and the Trained vs Untrained RSA in our predefined regions of interest. The anatomically defined vmPFC ROI showed higher similarity for matching identities versus mismatching ones (t_{28} = 2.76; p = 0.01), echoing the whole brain searchlight analysis. Neither the head (t_{28} = -1.22; p = 0.23) or the body (t_{28} = -0.21; p = 0.83) of the hippocampus showed significant multivariate effects of identity. Surprisingly, none of our regions of interest showed significantly higher similarity for the trained versus the untrained characters (all *ps* > 0.3).

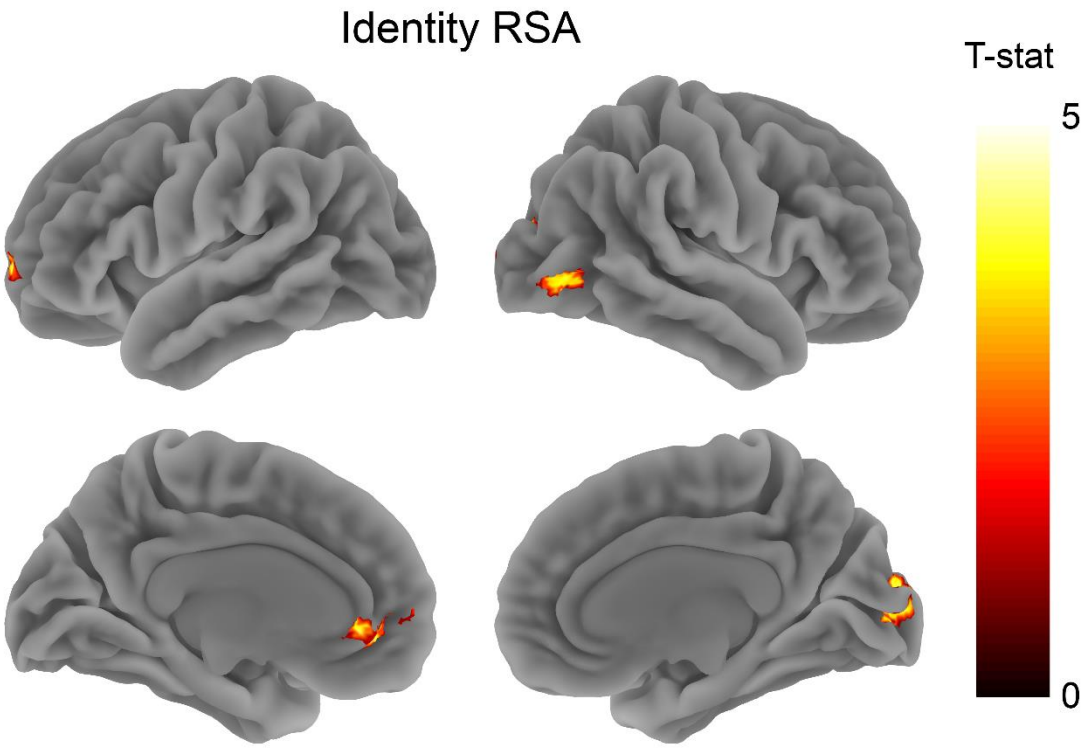

Figure 6 *Identity RSA.* Searchlight map shows regions that showed higher similarity for matching identities when compared to mismatching identities. Map is thresholded at $p < 0.001$ and FWE cluster size corrected.

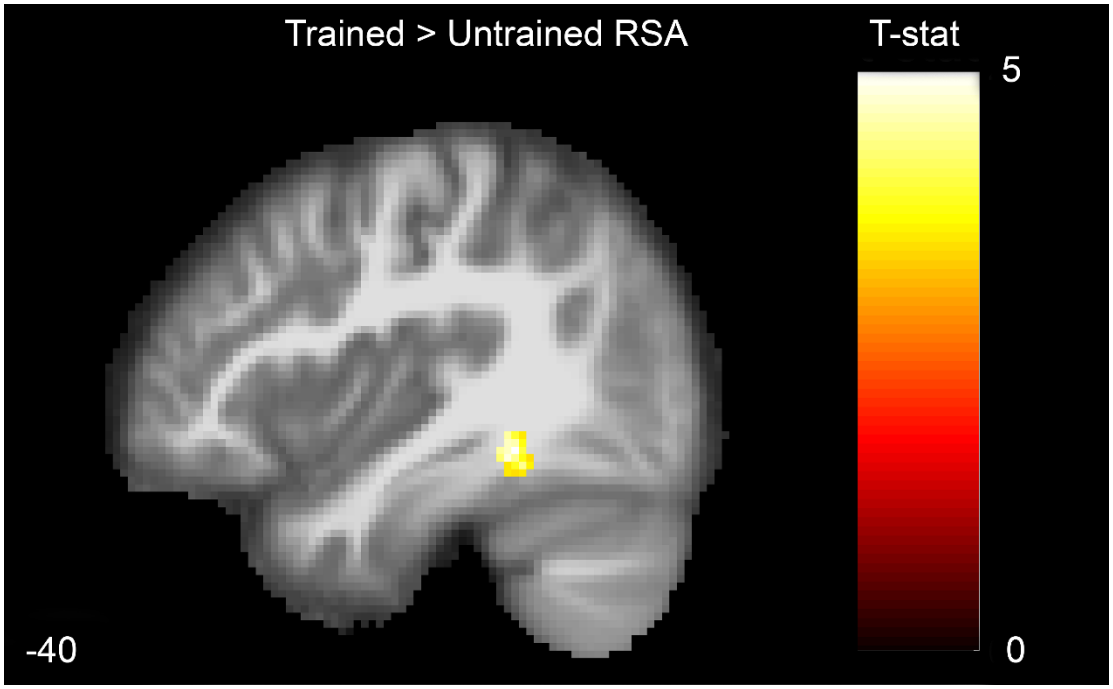

Figure 7 *Trained vs Untrained RSA*. Searchlight analysis revealed one region (the left fusiform gyrus) showing higher similarity for the trained identities when contrasted with the untrained identities. Map is thresholded at $p < 0.001$ and FWE cluster size corrected.

Discussion

The current study aimed to investigate the effects of recently acquired schematic knowledge on the processing of pictures of people. Before scanning we trained participants on one of two TV shows, which allowed us to examine brain regions that are associated with processing of knowledge that has been acquired across multiple occasions in a naturalistic manner. Whole-brain analyses revealed the vmPFC and retrosplenial cortex were more active when viewing trained versus untrained characters. To a lesser extent, but significant within our pre-specified regions of interest, both the head and the combined body and tail of the hippocampus also showed increased activation for the trained characters. We did not observe an inter-regional interaction between the vmPFC and the hippocampus suggesting a similar level of preference for the trained stimuli in both regions. Furthermore, we observed representational similarity identity effects in the vmPFC, but not in the hippocampus. Our results are consistent with theories implicating vmPFC and hippocampus in processing of schematic knowledge, but do not support a differential processing role for these regions in the face of prior knowledge.

Participants learned about the characters of a TV show over the course of a week. The training show was counterbalanced across participants allowing us to control for low-level visual differences between the shows and other potential confounds, such as the attractiveness or distinctiveness of the characters. Participants had to integrate information from multiple episodes to learn about the home, personalities, relationships and occupations of the main protagonists. This resembles how we acquire schematic knowledge in our everyday life and differentiates our design from previous studies that have relied on participants' pre-experimental knowledge without matching it across people or studies that have trained participants on rule-based associations. Furthermore, our design was different from other studies using naturalistic stimuli that have provided prior knowledge only specific to a single situation or narrative. Our finding of stronger activations in the vmPFC for the trained characters supports this region's proposed role in processing of schematic knowledge.

Notwithstanding the differences in study designs, our results are consistent with previous findings that have showed vmPFC involvement in prior knowledge effects (Baldassano et al., 2018; Kesteren et al., 2010; Liu et al., 2016; Preston & Eichenbaum, 2013; Tse et al., 2007, 2011; van Kesteren et al., 2013; Zeithamova et al., 2012). For instance, Liu et al., (2016) found higher vmPFC activation for famous versus non-famous faces (see also di Oleggio Castello et al., 2017; Von Der Heide et al., 2013). Using a weather prediction task trained over two days, (Wagner et al., 2015) observed higher vmPFC activity when participants were retrieving the rules after a 24-hour delay. Interestingly, lesions to the vmPFC have been associated with subtle schematic processing deficits (Ghosh et al., 2014). For instance, patients with vmPFC lesions have difficulty linking words ("receptionist") to their appropriate everyday schemas ("visit to the doctor") (Ghosh et al., 2014). Moreover, on word lists that contain thematically linked information ("bed", "tired", "rest", "dream"), healthy participants often have false memories for schematically linked but not presented targets ("sleep"). In contrast patients with vmPFC damage often do not make such false memory errors for schema congruent words (Ciaramelli et al., 2006; Melo et al., 1999; Warren et al., 2014). The paradoxically more accurate

performance of patients with frontal lesions could be due to their reduced ability to instantiate a schematic representation that biases the encoding of related words (see Gilboa & Marlatte, 2017).

We note that the orbitofrontal cortex, which overlaps with the vmPFC, is implicated in social cognition, in person-trait processing (Benoit et al., 2010; Jenkins et al., 2008; Krienen et al., 2010), and in representing stereotypes about people (Stolier & Freeman, 2016). These findings are compatible with a role for the region in schematic processing. Stereotypes and trait judgments are likely based on schematic-like knowledge acquired across multiple occasions. Future studies could test whether different types of schemas (e.g. social versus non-social) are more associated with different sub-regions of the medial prefrontal cortex. For instance, it is possible that vmPFC is more involved in prior knowledge when it involves social or evaluative aspects (see for similar suggestions Liu et al., 2016).

Apart from univariate training effects we found evidence for character-specific patterns of fMRI activity within the vmPFC, suggesting that the region contains information about people's identity. Interestingly, this effect was found for both the trained and the untrained characters. This finding is consistent with previous studies reporting successful identity decoding for both friends and unfamiliar others in the vmPFC (di Oleggio Castello et al., 2017). Surprisingly, we did not observe higher pattern similarity for trained identities versus untrained identities across runs. This might initially appear to be in contrast with the univariate effect in the vmPFC, however, it should be noted that correlation-based RSA analyses rely on the voxel level variability across conditions. On the other hand, univariate effects sensitive mainly to the mean activation differences across conditions (Davis et al., 2014). Future studies will be needed to better understand the neural coding mechanisms of schematic processing. One potential explanation for this pattern similarity finding is that the repeated exposure to the untrained characters allowed participants to make impressions about their identities (Todorov et al., 2015). Nevertheless, taken at face value, our RSA results, and the finding of di Oleggio Castello et al., (2017), are inconsistent with the view that the vmPFC plays a preferential role in processing stimuli associated with schema-related knowledge.

We also observed training effects on overall activation level in both the anterior (head) and posterior (body and tail) hippocampus. These effects were not significant at the whole-brain level but were present when considering average activity levels within the pre-defined ROIs. According to recent suggestions, these two sub-regions of the hippocampus process information at different levels. The posterior hippocampus is thought to process information at more detailed perceptual level, whereas the anterior hippocampus might support coarser gist-level semantic information (Poppenk et al., 2010; Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017). Based on these suggestions we might have expected that the anterior hippocampus might better differentiate between training conditions as it might reflect the gist-level information. Moreover, several studies contrasting responses to famous and non-famous faces have found effects in the anterior hippocampus and adjacent regions of the amygdala (Elfgren et al., 2006; Trinkler et al., 2009; Von Der Heide et al., 2013). However, our photo stimuli depicted not only the characters themselves, but also their apartments, which were familiar to participants after training. Since the posterior hippocampus is more associated with

processing spatial contexts (Nadel et al., 2013; Ranganath & Ritchey, 2012; Strange et al., 2014), this might explain why activity in this region was also modulated by training.

The higher hippocampal activation for the trained characters may be due to spontaneous reinstatement of episodic memories about the show (see also Ishai, 2008; Ishai et al., 2002; Trinkler et al., 2009), rather than simply the activation of associated schematic knowledge. This suggestion is in accordance with findings that famous names can be associated with personal memories (Renoult et al., 2012; Renoult et al., 2015; Westmacott et al., 2004; Westmacott & Moscovitch, 2003). This in turn might contribute to the (modest) boost in recognition performance for the pictures of trained individuals. Indeed, a number of studies have shown that learning new information which is related to prior experience was supported by the hippocampus (Liu et al., 2016; Poppenk et al., 2010; Preston et al., 2004; Sommer, 2016; Tse et al., 2007, 2011). However, the present study cannot provide direct evidence for the nature of the relationship between episodic recollection, schematic knowledge activation and memory for new information.

Some models propose that the hippocampus and vmPFC have competing roles. The SLIMM model proposes that the vmPFC monitors whether the current experience is related to prior schematic information and engages different memory processes depending on the amount of congruency with prior knowledge. By contrast, the medial temporal lobe, including the hippocampus, is involved in memory processing of novel information, but not of information strongly related to prior knowledge (van Kesteren et al., 2012). Therefore, according to the SLIMM model we might have expected to have seen stronger vmPFC response for the trained pictures and a stronger hippocampal response for the untrained pictures. In fact, we found that (1) the response in both the anterior and posterior hippocampus was greater for trained versus untrained pictures, and (2) that the trained versus untrained effects were not significantly different between the vmPFC or either hippocampal ROI. These findings are inconsistent with the SLIMM model. However, our findings are consistent with other studies reporting increased hippocampal involvement for prior knowledge effects from a range of tasks (Liu et al., 2016; Sommer, 2016; Zeithamova et al., 2012). More broadly, our findings lend support to accounts of memory processing that view the roles of the vmPFC and hippocampus as being complementary (e.g. Robin & Moscovitch, 2017) or working together under situations with moderate levels of prior knowledge (Gilboa & Marlatte, 2017).

Given that prior schematic knowledge modulates activity in the vmPFC and hippocampus to a similar degree, future studies will be needed to better understand the nature of their roles in schema-based semantic and episodic memory processes. For example, both the vmPFC and the hippocampus have been shown to be involved in episodic memory retrieval (e.g. see McCormick et al., 2018). However, they seem to process information at different levels of abstraction. Partial damage to hippocampal regions is associated with loss of detailed memories, but preserved gist, or story level memories (St-Laurent et al., 2014). On the other hand, damage to vmPFC is often associated with problems in schematic processing (Ciaramelli et al., 2006; Melo et al., 1999; Spalding et al., 2015; Warren et al., 2014). Nonetheless, it is important to note that schematic processing has rarely been examined in patients with hippocampal damage and more research is needed to understand how vmPFC

lesions affect episodic memory (see McCormick et al., 2018 for review). An open question for future studies is to examine to what extent encoding of new information related to prior schematic knowledge depends on episodic memory retrieval (see Zeithamova et al., 2012).

Beyond the effects in the vmPFC and hippocampus, two further regions warrant mention. First, there was an increase in activation for pictures of trained versus untrained characters in the retrosplenial cortex. Posterior midline regions including the retrosplenial cortex are strongly implicated in processing known versus unknown entities (e.g. Liu et al., 2016; Von Der Heide et al., 2013) and are also frequently identified in studies that have manipulated prior knowledge (e.g. Ames et al., 2015; Maguire et al., 1999). Although posterior midline regions have attracted less attention than the vmPFC in schema processing, it is possible that they nevertheless play an important role in linking incoming information with prior knowledge (see also Bird et al., 2015). The second region is the left fusiform gyrus, as this was the only brain region in our study to show significant identify-specific RSA effects that were greater for trained compared to untrained characters. This is a region strongly implicated in face processing (Kanwisher et al., 1997) and other studies that have examined prior knowledge for faces have also often observed effects here (e.g. see Brod et al., 2016; Liu et al., 2016; Schlichting & Preston, 2016). Interestingly, a study by Axelrod & Yovel (2015) also found that a region in the fusiform gyrus was the only place where the identify of famous faces could be decoded from patterns of BOLD activity. The mechanism underpinning these findings is unclear, but it is possible that familiarity with a person "sharpens" the representation in this region, resulting in increased pattern similarity. Follow-up studies could examine whether different types of category-specific schematic knowledge result in representational similarity effects in other specialised cortical regions (e.g. locations in the parahippocampal gyrus).

It may seem surprising that we did not observe more widespread RSA effects of location. Only one region (within the left postcentral gyrus) showed greater similarity for the same compared with different locations. However, it should be noted that all of the locations were highly similar – all being apartments belonging to a young married couple. Although the locations could be living rooms or kitchens, during the training episodes participants saw a lot of scenes involving the characters moving from one to another. This could have led to a highly associated representation of these locations. Our result contrasts with studies that have observed robust and widespread location similarity effects, which have often used locations that are distinctive and unique to different episodes (e.g. Robin et al., 2018). Furthermore, the participants' task was to detect the oddball pictures of elderly individuals, which potentially directed their attention more to the faces present in the picture rather than the locations.

In sum: our results further support the neurocognitive theories that suggest a role for both the vmPFC and hippocampus in schema-based processing of new information and they also identify the posterior midline cortex in as an additional region associated with person-specific schematic knowledge. Our study employed a novel paradigm to enable participants to acquire novel schema in a naturalistic manner. New schematic knowledge boosted performance on tests of episodic memory for previously unseen pictures and short videos. The finding that prior

knowledge increased activity in both the vmPFC and the hippocampus to similar extent is at odds with the SLIMM account of memory processing. Future studies are needed to establish the effects of the specific content and richness of schema knowledge on the involvement of particular brain areas.

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Supplementary Materials

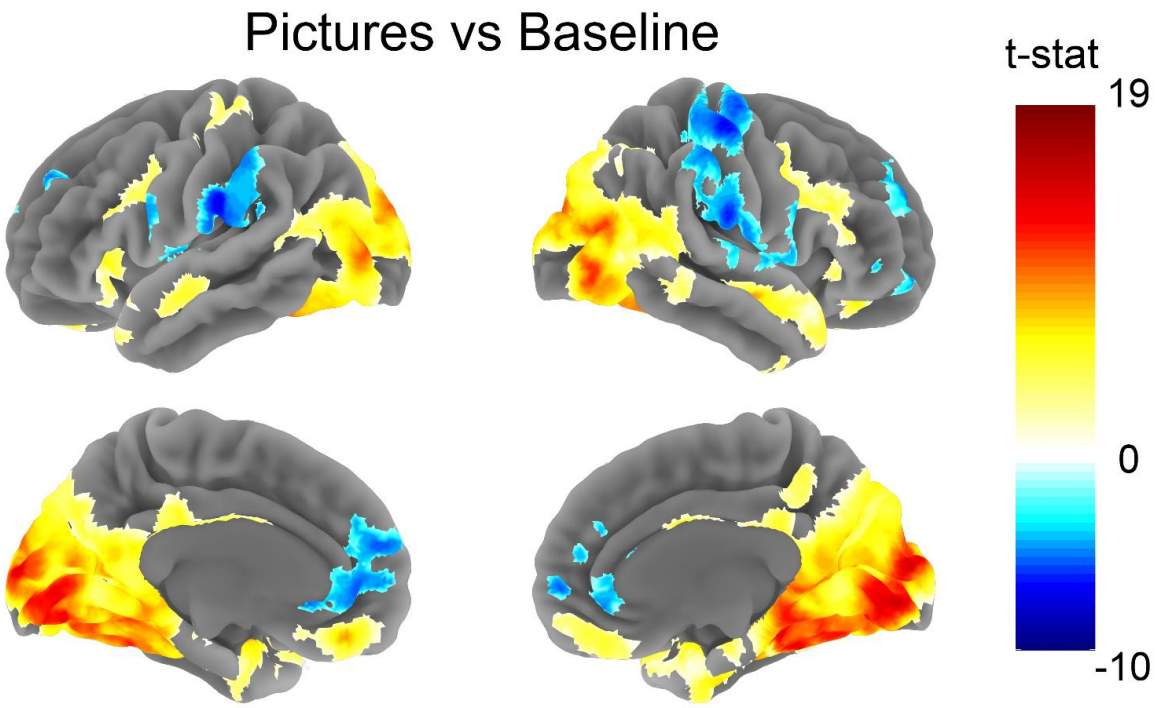

Figure 1 Brain regions with higher activation for watching pictures (both trained and untrained) versus the odd-even number judgment baseline task. The map is FWE cluster corrected with a voxel threshold $p < 0.001$.

A Stranger's Death				
	Who did Dharma Meet?	**1. George**	2. David	3. Britney
	Where did she meet him?	1. On the street	2. In their apartment	**3. On the roof**
	Why does he have to die here?	1. Because it is where he was born	2. Because it is his old place	**3. Because the spirits could guide his soul**
	How does Dharma respond when Greg says it is incredible	**1. She says it is awesome**	2. She says it sounds bad	3. She argues with him
	What is Greg wearing?	**1. A suit**	2. A T-shirt	3. Winter Jacket

Figure 2 Example questions for a single video clip. The title indicates for which video the questions are. The participants see each question one after the other and have to make a choice between three provided options. The highlighted options are the correct answers (they were not presented to the participants).